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"A therapeutically useful compound"

"Terapeuttisesti hyödynnettävä yhdiste"

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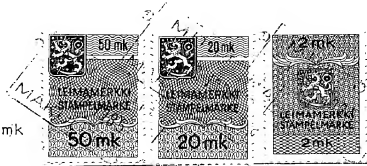

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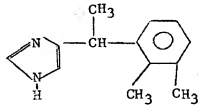
A therapeutically useful compound

This invention relates to the use of 4-[(α -methyl)-2,3-dimethylbenzyl]imidazole as a sedative-analgesic agent in the veterinary field.

The compound 4-[(α-methyl)-2,3-dimethyl-benzyl]imidazole having the formula



(I)

has been previously disclosed in the European Patent Publication no 72615 as an antihypertensive agent.

The compound 4-(2,3-dimethylbenzyl)-imidazole or detomidine is a known compound with a sedative and analgesic effect in horses and cattle. Detomidine is used in veterinary medicine as a pharmacological restraint whereby the animal is sedated before investigation, treatment and difficult medical operations. Even a small surgical operation cannot be carried out without the use of a sedative agent.

The effect of detomidine in horses and cattle has been described in the literature, e.g. O. Vainio: "Detomidine hydrochloride – a novel imidazole -type sedative-analgesic". Pharmacologie et Toxicologie Veterinaires, INRA Publ. Paris, 1982, Les Colloques de I'INRA, no 8.

There is also a great need for sedative-analgesic agents as pharmacological restraints in the treatment of dogs, cats and other small animals. Detomidine was tested on these animals, but no useful effect could, however, be observed.

We have now surprisingly found that the detomidine analoque, 4-[(α-methyl)-2,3-dimethylbenzyl]imidazole (compound (I)) is very effective as a sedative-analgesic in the treatment of small animals, especially dogs and cats, but also e.g. quinea pigs and rabbits.

Intramuscular or intravenous administration of this compound at a dose of 10 to 160 µg/kg (dogs and cats) or 200 to 400 µg/kg (quinea pigs and rabbits) induces a sedative effect which appears in 2 to 10 minutes after intramuscular administration or in 0.5 to 1 min. after intravenous administration. Both the strength and the duration of the effects are clearly dose dependant higher doses having a hypnotic effect during which the animals do not react to external stimuli as sounds, pain etc. The duration of the effect is about 1 to 4 hours in dogs and 0.5 to 2 hours in cats. Sedation is accompanied with an analgesic effect, especially at higher doses.

This compound posesses both a sedative and an analgesic effect, which are clearly superior to those of xylazine, which is a known compound commonly used as sedative in the treatment of small animals.

The following test data illustrate the invention. The tests were carried out using six beagle dogs per group. The study was carried out using a cross-over-design.

Different doses of compound (I) were given i.m. or i.v.. The reactions observed were compared to obtained by xylazine.

Table 1: Reaction to sounds

	compound (I)						xylazine			
dose, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v
results (number of dogs):										
normal reaction	–	1	–	–	–	–	6	4	2	2
weak reaction	3	–	–	–	1	1	–	2	3	4
no reaction	3	5	6	6	5	5	–	–	1	–
total number of dogs	6	6	6	6	6	6	6	6	6	6

Table 2: Duration of the sedation

	compound (I)						xylazine			
dose, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v
duration:										
0 – 15 min	–	–	–	–	–	–	4	2	2	1
15 – 30 min	2	2	–	–	–	–	2	4	3	4
30 – 60 min	4	4	3	4	1	2	–	–	1	1
1 – 2 h	–	–	3	2	3	3	–	–	–	–
> 2 h	–	–	–	–	2	1	–	–	–	–
total number of dogs	6	6	6	6	6	6	6	6	6	6

Table 3: First signs of sedation

	mean, min		variation, min	
	i.m.	i.v.	i.m.	i.v.
compound (I), 40 µg/kg	5	0.7	3 – 10	0.5 – 1
compound (I), 80 "	3	0.6	2 – 6	0.5 – 1
compound (I), 160 "	2	0.5	2 – 3	0.5 – 0.5
xylazine, 1500 µg/kg	4	2	2 – 8	0.5 – 10
xylazine, 3000 "	2	0.5	2 – 3	0.5 – 0.5

Table 4: Evaluation of the sedative effect

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v
no activity	–	–	–	–	–	–	–	–	–	–
some activity	–	1	–	–	–	–	6	6	2	3
good activity	6	5	6	6	6	6	–	–	4	3
total no of dogs	6	6	6	6	6	6	6	6	6	6

Table 5: Evaluation of the analgesic effect

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v
no activity	–	–	–	–	–	–	–	–	–	–
some activity	1	3	–	–	–	–	6	6	4	5
good activity	5	3	6	6	6	6	–	–	2	1
total no of dogs	6	6	6	6	6	6	6	6	6	6

Table 6: The position of the animal during the maximum effect

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v
position: standing	–	–	–	–	–	–	1	–	–	–
able to get up easily	–	–	–	–	–	–	4	4	2	2
able to get up with difficulty	3	3	1	–	–	1	1	2	4	4
not able to get up	3	3	5	6	6	5	–	–	–	
total no of dogs	6	6	6	6	6	6	6	6	6	6

Claims

1. The use of the compound 4-[(α-methyl)-2,3-dimethylbenzyl]-imidazole as veterinary sedative-analgetic agent.

2. The use according to claim 1 wherein small animals as dogs, cats, quinea pigs, rabbits and the like are treated.

Abstract

This invention relates to the use of the compound 4-[(α-methyl)-2,3-dimethyl-benzyl]imidazole as a veterinary sedative-analgetic agent.